

REMARKS

In Response to the Restriction Requirement of September 27, 2001, Applicants elected the Claims in Group I with traverse. Also, in this Response mailed December 18, 2001, Applicants cancelled Claims 12-16 and added new Claims 17-21, in order to correct a numbering error in the application as originally filed. As Applicants indicated in the Response to the Restriction Requirement, there was no Claim 12 in the application as originally filed (*i.e.*, the application was originally filed with Claims 1-11, and 13-16). Thus, Applicants submit that by canceling Claims 12-16 and adding Claims 17-21, Applicants were in compliance with 37 C.F.R. 1.126, as the original numbering of the Claims was preserved and the new Claims added in the Response to the Restriction Requirement began with the next consecutive number (*i.e.*, Claim 17). Thus, Applicants respectfully submit that the Claims as filed and indicated in the Response to the Restriction Requirement were correct. Thus, Claims 1-7, 9-11 and 17-21 (*i.e.*, not Claims 16-20, as indicated by the Examiner) are currently pending.

In order to further the prosecution of the present application and their business interests, Applicants have cancelled Claim 21, directed toward a cleaning composition, as the Examiner has indicated that this Claim belongs in a non-elected Group. Thus, Claims 1-7, 9-11 and 16-20 are currently pending. Applicants reserve the right to pursue Claim 21 in a subsequent filing. Applicants have also corrected the informalities in Claims 3 and 10. The Examiners rejections of the Claims are addressed in the order below:

- 1) Claims 1-7, 9-11 and 16-19 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not meeting the written description requirement;
- 2) Claims 1-7, 9-11 and 16-19 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not being enabled;
- 3) Claims 1-7 and 9-10 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite;

4) Claims 1-7, 9-10 and 18 stand rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Band *et al.*; and

5) Claims 11 and 16-19 stand rejected under 35 U.S.C. §103(a) as being allegedly obvious under Band *et al.*, in view of Sloma *et al.* and Power *et al.*

**1) The Present Application and Claims Meet the
Written Description Requirement**

The Examiner has rejected Claims 1-7, 9-11 and 16-19, under 35 U.S.C. §112, first paragraph, as allegedly not meeting the written description requirement. More particularly, the Examiner indicates that the Claims are drawn to a genus of serine protease 1 genes, with any structure and from any source. Applicants note that the Examiner admits that the Specification teaches serine protease 1 from *Bacillus subtilis* (SEQ ID NO:1). The Examiner argues that teaching one representative species is not enough to describe the whole genus and there is no evidence of the relationship between the structure of *B. subtilis* serine protease 1 and the structure of a serine protease from another source. Applicants must respectfully disagree with the Examiner's arguments and believe that the Specification as filed meets the written description requirement. Nonetheless, in order to further the prosecution of the present application and their business interests, yet without acquiescing to the Examiner's arguments, Applicants have amended independent Claims 1, 9 and 11, to recite SEQ ID NO:1. Applicants submit that the Claims are supported by the Specification (*i.e.*, no new matter is introduced by this amendment) and meet the written description requirement. Applicants respectfully request that this rejection be withdrawn.

2) The Claims are Enabled

The Examiner has rejected Claims 1-7, 9-11 and 16-19 under 35 U.S.C. §112, second paragraph, as allegedly being non-enabled. The Examiner argues

that the Specification "does not reasonably provide enablement for a serine protease 1 gene not homologous to SEQ ID NO:1." (Office Action, page 4). Applicants must respectfully disagree. Applicants also note that the Examiner admits that the Specification is enabling for the nucleic acid encoding serine protease 1 of SEQ ID NO:1. While not acquiescing to the Examiner's arguments, but in order to further the prosecution of the present application and their business interests, Applicants have amended independent Claims 1, 9 and 11, to recite SEQ ID NO:1. Applicants reserve the right to pursue the originally filed and/or similar Claims in a subsequent filing. As the amended Claims recite SEQ ID NO:1, Applicants submit that the Claims are enabled and respectfully request that this rejection be withdrawn.

3) The Claims are Definite

The Examiner has rejected Claims 1-7 and 9-10, under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The Examiner indicates that the mere recitation of "SP1" is insufficient to convey with clarity that which Applicants view as their invention. Applicants have amended independent Claims 1 and 9 to recite "serine protease 1," in addition to the abbreviation "SP1," in order to more clearly describe the presently claimed invention. Thus, Applicants submit that the Claims are definite and respectfully request that this rejection be withdrawn.

4) The Claims are Novel

Claims 1-7, 9-10 and 18 stand rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Band *et al.* The Examiner argues that Band *et al.* teach a *Bacillus subtilis* having a mutated gene encoding a serine protease-1, resulting in the inactivation of the proteolytic activity of the enzyme. As indicated above, in order to further the prosecution of the present application and their business interests, yet without acquiescing to the Examiner's arguments,

Applicants have amended independent Claims 1 and 9 to recite SEQ ID NO:1. There is no teaching in Band *et al.* reference of the sequence set forth in SEQ ID NO:1. Thus, as the Band *et al.* reference does not teach each and every element of the Claims², a requirement for a reference to be anticipatory, this rejection should be withdrawn. Applicants respectfully request that this rejection be withdrawn and the Claims passed to allowance.

5) The Claims are Unobvious

Claims 11 and 16-19 stand rejected under 35 U.S.C. §103(a) as being allegedly obvious under Band *et al.*, in view of Sloma *et al* and Power *et al.* The Examiner indicates that Band *et al.* teaches a *B. subtilis* having a mutation in the gene encoding serine protease-1, which results in the inactivation of its proteolytic activity. However, the Examiner admits that the Band *et al.* reference does not teach a microorganism comprising a mutated serine protease 1 gene further comprising a mutated *epr* gene nor a method of producing a heterologous protein using said microorganism.

The Examiner indicates that Sloma *et al.* teach a *B. subtilis* comprising a mutated *epr* gene, while Power *et al.* teach a method of producing heterologous proteins, such as a lipase in *Bacillus*. The Examiner argues that it would have been obvious "to make a *B. subtilis* comprising a mutated serine protease 1 gene and a mutated *epr* gene and to use the microorganism in production and secretion [of] heterologous lipases without proteolytic degradation. The motivation of using such a host system with the mutate [sic] proteases is to decrease proteolytic activity during the production and secretion of the heterologous protein. One of ordinary skill in the art would have had a reasonable expectation of success since recombinant production of

² "Anticipation is established only when a single prior art reference discloses, expressly or under principles of inherency, each and every element of a claimed invention." *RCA Corp. v. Applied Digital Data Sys., Inc.*, 730 F.2d 1440, 221 USPQ 385, 388 (Fed. Cir. 1984).

heterologous proteins in *Bacillus* is routinely performed in the art.” (Office Action, pages 7-8). Applicants respectfully traverse because a *prima facie* case of obviousness is not established. Applicants submit that a *prima facie* case of obviousness requires the Examiner to cite to a combination of references which (a) suggests or motivates one of skill in the art to modify their teachings to yield the claimed invention, (b) discloses the elements of the claimed invention, **and** (c) provides a reasonable expectation of success should the claimed invention be carried out. Failure to establish **any** one of these requirements precludes a finding of a *prima facie* case of obviousness and, without more, entitles Applicants to withdrawal of the rejection of the Claims in issue.³ Applicants urge that the Examiner has failed to establish not one, but **all three** requirements, as discussed below.

First, none of the references teach each and every element of the amended Claims. None of the cited references teach the sequence set forth in SEQ ID NO:1. As the references fail to teach each and every limitations of the rejected claims, a *prima facie* case of obviousness is not established. This alone necessitates withdrawal of the rejection of the claims under 35 U.S.C. §103.

The Examiner argues that motivation exists with respect to each of the rejected Claims in the production of heterologous proteins without proteolytic degradation. However, the combination of the cited references does *not* provide the presently claimed invention, as the sequence of the serine protease 1 claimed is not provided by the cited prior art. Thus, even if the references are combined, the presently claimed invention is not produced and another prong of a *prima facie* case of obviousness is not met.

Finally, a fundamental requisite of establishing a *prima facie* case of obviousness is that there is a reasonable expectation of success in obtaining the

³See e.g., *Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990); *In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988).

claimed invention. In addition, "the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure."⁴ The Examiner has not advanced a single argument nor any evidence to establish that one skilled in the art would have had a reasonable expectation of success in obtaining the presently claimed invention, which includes the recitation of SEQ ID NO:1. This omission negates a *prima facie* case of obviousness, and entitles Applicant to allowance of the claims in issue.

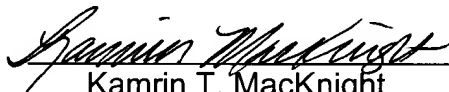
Because, not one, but each of the **three** elements of a *prima facie* case of obviousness remains lacking, a *prima facie* case of obviousness cannot be established. It is therefore respectfully requested that the rejection of Claims 11, and 16-19, under 35 U.S.C. §103(a) for alleged obviousness be withdrawn.

CONCLUSION

All grounds of rejection and objection of the Office Action of January 3, 2002, having been addressed, reconsideration of the application is respectfully requested. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourages the Examiner to call the undersigned.

Respectfully submitted,

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⁴*In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988) as cited in *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

APPENDIX I
MARKED-UP VERSION OF SPECIFICATION'S REPLACEMENT
PARAGRAPHS AND REWRITTEN, ADDED, AND/OR CANCELLED CLAIMS

The following is a marked-up version of the Specification's replacement paragraphs pursuant to 37 C.F.R. §1.121(b), as well as a marked-up version of the Claims pursuant to 37 C.F.R. §1.121 (c)(1)(ii) with instructions and markings showing changes made herein to the previous version of record of the Specification and Claims. Underlining denotes added text while bracketing denotes deleted text.

Please cancel Claim 21.

1. (Amended) A gram-positive microorganism having a mutation or deletion of part or all of the gene encoding serine protease 1 (SP1), wherein said gene encoding serine protease 1 comprises SEQ ID NO:1, said mutation or deletion resulting in the inactivation of the SP1 proteolytic activity.

2. (Amended) The gram-positive microorganism according to Claim 1 that is a member of the [family] genus Bacillus.

3. (Amended) The microorganism according to Claim 2, wherein the member is selected from the group consisting of B. licheniformis, B. lentus, B. brevis, B. stearothermophilus, B. alkalophilus, B. amyloliquefaciens, B. coagulans, B. circulans, B. lautus and Bacillus thuringiensis [B. licheniformis, B. lentus, B. brevis, B. stearothermophilus, B. alkalophilus, B. amyloliquefaciens, B. coagulans, B. circulans, B. lautus and *Bacillus thuringiensis*] .

5. (Amended) The microorganism of Claim 4, wherein said heterologous protein is selected from the group consisting of hormones, enzymes, growth factors and cytokines.

7. (Amended) The microorganism of Claim 6, wherein said enzyme is selected from the group consisting of [a] proteases, carbohydrases, [and] lipases[:]; isomerases, [such as] racemases, epimerases, tautomerases, [or] mutases[:]; transferases, kinases, and phosphatases.

9. (Twice Amended) An expression vector comprising nucleic acid encoding SP1, wherein said SP1 comprises the nucleic acid sequence set forth in SEQ ID NO:1.

10. (Amended) A host cell comprising an expression vector according to Claim 9.

11. (Twice Amended) A method for the production of a heterologous protein in a *Bacillus* host cell comprising the steps of

(a) obtaining a *Bacillus* host cell comprising nucleic acid encoding said heterologous protein wherein said host cell contains a mutation or deletion in the gene encoding serine protease 1, wherein said serine protease 1 comprises the nucleic acid sequence set forth in SEQ ID NO:1;

(b) growing said *Bacillus* host cell under conditions suitable for the expression of said heterologous protein.

17. The method of Claim 11 wherein said *Bacillus* cell is selected from the group consisting of *Bacillus subtilis*, *B. licheniformis*, *B. lentus*, *B. brevis*, *B. stearothermophilus*, *B. alkalophilus*, *B. amyloliquefaciens*, *B. coagulans*, *B. circulans*, *B. lautus* and *Bacillus thuringiensis*.

18. (Amended) The method of Claim 17 wherein said *Bacillus* [Bacillus] host cell further comprises a mutation or deletion in at least one of the genes encoding apr, npr, epr, wpr and mrp.

19. (Amended) A gram-positive microorganism having at mutation or deletion in the gene encoding serine protease 1, wherein said serine protease 1 is encoded by the nucleic acid set forth in SEQ ID NO:1.